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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,001	12/21/2001	Charles A. Nicolette	GZ 2108.00	5913

7590 12/30/2004

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EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/026,001

Applicant(s)

NICOLETTE, CHARLES A.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 5-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 03/14/02, 03/12/03, 04/02/03

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Exhibit A (Seq. Alignment)

DETAILED ACTION

Election/Restrictions

Applicant's election of group I encompassing claims 1-4, drawn to compositions comprising a protein and peptides in the reply filed on 10/20/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1-40 are pending, and claims 1-4 are examined on merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the same native ligand" in line 3. There is insufficient antecedent basis for this limitation in the claim. For compact prosecution purpose, the Office assumes "the same native ligand" to be a human cytokeratin 18 (CK18) for art search purpose, since the specification discloses cytokeratin 18 (CK18) only as an native ligand. However, this treatment does not relieve applicant the burden of responding this rejection.

The dependent claims 2-4 are also rejected because the dependent claims include the rejected limitation, but do not further clarify the rejected limitation.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, and 2 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, and 2, as written, do not sufficiently distinguish over nucleic acids, as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" in front of "immunogenic ligand" in line 1 of claims 1, and 2. See MPEP 2105.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 95/31728 (23 November 1995, #9 of IDS filed on 03/11/2003).

Claims 1-4 are interpreted as drawn to a composition comprising at least one immunogenic ligand, wherein said immunogenic ligand is selected from an immunogen

comprising SEQ ID NOs: 3, 5, or 7, wherein said ligand elicit an immune response against CK18 (the base claim 1), wherein said composition of the base claim further comprises an immunogenic portion of SEQ ID NO:1 (claim 2), wherein said composition comprises a carrier. Since the claims 1-3 as currently construed do not have a transitional phrase (note the limitation “selected from the group consisting of SEQ ID NOs:3, 5, and 7” in line 4 of claim 1 is a Markush format indicating the alternate choice, not a transitional phrase), the scope of the claimed “immunogenic ligand” is broadly interpreted as drawn to an immunogen **comprising** SEQ ID NO:7.

WO 95/31728 at pages 15-18, Examples 4-6, teaches a composition, i.e. “immunogen” comprising immunogenic ligand, wherein said immunogenic ligand comprising SEQ ID NO:7 (note lines 26-28 of page 15 “fusion proteins consisting of 260 amino acids of the T7 gene 10 protein and amino acids 140-430 of human CK18”, which comprises the instant SEQ ID NO:7, i.e. the 10-mer polypeptide of FMKKNHEEEV, and also comprises an immunogenic portion of SEQ ID NO:1 according to the sequence search result from the protein database PIR, note Exhibit A (the sequence alignment of instant SEQ IS NO:1 against Genbank accession number S05481, i.e. the human keratin 18), which shows that amino acids #140-430 of human CK18 comprises instant SEQ ID NO:7. WO 95/31728 especially Example 5 at page 16-17, Table 4 teaches that the antibodies produced by the composition comprising the immunogen reacts to CK18 present in blood samples from a human subject, and cancer patients, thus the immunogen of WO 95/31728 has “ability to elicit an immune response against the same native ligand”. As for “a carrier” in claim 3, and a pharmaceutically acceptable carrier in

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claim 4, the immunogen comprising the fusion proteins consisting of 260 amino acids of the T7 gene 10 protein and amino acids 140-430 of human CK 18 being injected into Balb/c mouse inherently has a pharmaceutically acceptable carrier because it is the Office's position that injection of immunogen into in vivo subject inherently has "a pharmaceutically acceptable carrier" Note the broad definition of the specification at paragraph [0108] for the term "pharmaceutically acceptable carrier" as encompassing "any of the standard pharmaceutical carriers, such as a phosphate buffered saline solution, water, and emulsions, such as an oil/water or water/oil emulsion, and various types of wetting agents. The compositions also can include stabilizers and preservatives."

WO 95/31728 does not disclose amino acids of cytokeratin-18, however, cytokeratin-18 of WO 95/31728 patent appears to possess the same structure and same function as the instantly claimed invention. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the composition of the prior art does not possess the same material, structural and functional characteristics of the instantly claimed composition. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed composition is different from those taught by the prior art and to establish patentable differences. See *In re Best* 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat. 5,780,032 (14 July 1998, #1 of IDS filed on 03/11/2003).

Claims 1-4 are interpreted as drawn to a composition comprising an immunogenic ligand, wherein said immunogenic ligand is selected from an immunogen comprising SEQ ID NO: 7, wherein said ligand elicit an immune response against CK18 (the base claim 1), wherein said composition of the base claim further comprises an immunogenic portion of SEQ ID NO:1 9 (claim 2), wherein said composition comprises a carrier, wherein a said carrier is a pharmaceutically acceptable carrier (claim 4). Since the limitation “selected from the group consisting of SEQ ID NOs:3, 5, and 7” in line 4 of claim 1 is a Markush format indicating the alternate choice, not a transitional phrase, the scope of an immunogenic ligand is broadly interpreted as drawn to a composition comprising an immunogen comprising SEQ ID NO:7.

US Pat. 5,780,032 teaches a composition comprising cytokeratin 18 in PBS at column 3, lines 27-29. Note the attached sequence alignment (Exhibit A) showing that cytokeratin 18 comprises instant SEQ ID NO:7 in the middle of the 430 amino acid protein, and cytokeratin 18 is identical to instant SEQ ID NO:1. The ‘032 patent teaches that the fragments from the cytokeratin could be used as immunogen i.e., the protein fragments can elicit an immune response against cytokeratin-18 (note abstract, Fig. 1, and 18 for example).

The ‘032 patent does not disclose amino acids of cytokeratin-18, however, cytokeratin-18 of the 032 patent appears to possess the same structure and same function as the instantly claimed invention. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the composition of the prior art does not possess the same material, structural and functional characteristics of the instantly claimed composition. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed composition is different from those taught by the prior art and to establish patentable differences.

See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

A handwritten signature in black ink, appearing to read 'Misook Yu', with a stylized flourish at the end.

QY 121 PVRDMSHYFKIIEEDLRAQIFANTVDNARIVLQIDNARLAADDFRVKYTELAMROSVEN 180
DB 121 PVRDMSHYFKIIEEDLRAQIFANTVDNARIVLQIDNARLAADDFRVKYTELAMROSVEN 180
QY 181 DIHGLRKVIDDNTNITRLQLETEIEALKEELLFMKKNHEEVEVKGLQAOIASGGLTVEVDAP 240
DB 181 DIHGLRKVIDDNTNITRLQLETEIEALKEELLFMKKNHEEVEVKGLQAOIASGGLTVEVDAP 240
QY 241 KSQDLAKIMADIRAOYDELAARKNREELDKYWSQOIEESTVVTQSAAVGAETTLTELK 300
DB 241 KSQDLAKIMADIRAOYDELAARKNREELDKYWSQOIEESTVVTQSAAVGAETTLTELK 300
QY 301 RTVQSLIEDLDSMRNLKASLENSLREVEARYALQMEQNGILHLHSESLAQTRAEGGROA 360
DB 301 RTVQSLIEDLDSMRNLKASLENSLREVEARYALQMEQNGILHLHSESLAQTRAEGGROA 360
QY 361 QEYEAALNKKVLEAEIATYRRLLEDGEDFNLGDALDSNSMOTIOKTTTRRIVDGKRV 420
DB 361 QEYEAALNKKVLEAEIATYRRLLEDGEDFNLGDALDSNSMOTIOKTTTRRIVDGKRV 420
QY 421 ETNDTKVLRH 430
DB 421 ETNDTKVLRH 430

RESULT 2

159463

keratin, type I, cytoskeletal - mouse

M/Alternate names: endo B cytokekeratin; keratin D

C/Species: Mus musculus (house mouse)

C/Date: 02-Aug-1996 #sequence revision 02-Aug-1996 #text_change 09-Jul-2004

C/Accession: 159463; A25621; A28428; J04046

R/Alonso, A.; Weber, T.; Jorcano, J.L.

Roux's Arch. Dev. Biol. 196, 16-21, 1987

A/Title: Cloning and characterization of keratin D, a murine endodermal cytoskeletal pro

A/Reference number: 159463

A/Accession: 159463

A/Status: preliminary; translated from GB/EMBL/DBJ

A/Molecule type: mRNA

A/Residues: 1-423 <RES>

A/Cross-references: UNIPROT:P05784; GB:M36376; NID:g198587; PIDN:AAA39373.1; PID:g293682

R/Singer, P.A.; Trevor, K.; Oshima, R.G.

J. Biol. Chem. 261, 538-547, 1986

A/Title: Molecular cloning and characterization of the endo B cytokekeratin expressed in F

A/Reference number: A25621; MUID:86085876; PMID:2416755

A/Accession: A25621

A/Molecule type: mRNA

A/Residues: 1-243, 'D', 245-252, 'A', 254-423 <SIN>

A/Cross-references: GB:M11686; NID:g198620; PIDN:AAA39390.1; PID:g293685

R/Oshima, R.G.; Trevor, K.; Shevinsky, L.H.; Ryder, O.A.; Cecena, G.

Genes Dev. 2, 505-516, 1988

A/Title: Identification of the gene coding for the endo B murine cytokekeratin and its me

A/Reference number: A28428; MUID:88255838; PMID:2454868

A/Accession: A28428

A/Molecule type: DNA

A/Residues: 1-132 <OSH>

A/Cross-references: GB:Y00217; NID:g50842; PIDN:CAA68365.1; PID:g50843

R/Johnson, Y.; Morita, T.; Zhang, F.; Srimahasongram, S.; Tondella, M.L.C.; Matsumoto,

Gene 70, 85-95, 1988

A/Title: Nucleotide sequence and structure of the mouse cytokekeratin endoB gene.

A/Reference number: J04046; MUID:89196920; PMID:2467843

A/Accession: J04046

A/Molecule type: DNA

A/Residues: 1-133, 'F', 135-243, 'D', 245-252, 'A', 254-423 <ICH>

A/Cross-references: GB:M22832; NID:g340757; PIDN:AAA37552.1; PID:g532610

C/Genetics:

A/Gene: endoB; KERD

A/Introns: 132/3; 160/2; 212/3; 267/3; 309/3; 384/2

C/Superfamily: cytoskeletal keratin

C/Keywords: coiled coil; intermediate filament

Query Match 85.3%; Score 1808.5; DB 2; Length 423;
Best Local Similarity 85.6%; Pred. No. 2.5e-81;

Matches 370; Conservative 27; Mismatches 24; Indels 11; Gaps 4;
QY 1 MSFTTRS-TFSTNYSRLSGVQAPSYGAPVSSAASVYAGAGSGSRSISVRSSTFRGGMG 59
DB 1 MSFTTRSTFSTNYSRLSGVQAPSYGAPVSSAASVYAGAGSGSRSISVRSV-WGSSVG 59
QY 60 SGGGLATGAGLAGMGGIONEKETMOSLNDRLASVLDVRVSLTEENRRLSKIREHLEKK 119
DB 60 S-----AGLAGMGGIQTEKETMQLNDRLASVLDKVKSLTEENRRLSKIREHLEKK 111
QY 120 GPD-VRDMSHYFKIIEEDLRAQIFANTVDNARIVLQIDNARLAADDFRVKYTELAMROS 178
DB 112 GPQVPRDMSHYFKIIEEDLRAQILANSVDNARIVLQIDNARLAADDFRVKYTELAMROS 171
QY 179 ENDHGLRKVIDDNTNITRLQLETEIEALKEELLFMKKNHEEVEVKGLQAOIASGGLTVEVD 238
DB 172 ESDHGLRKVIDDNTNITRLQLETEIEALKEELLFMKKNHEEVEVKGLQAOIASGGLTVEVD 231
QY 239 APKSQDLAKIMADIRAOYDELAARKNREELDKYWSQOIEESTVVTQSAAVGAETTLTE 298
DB 232 APKSQDLAKIMADIRAOYDELAARKNREELDKYWSQOIEESTVVTQSAAVGAETTLTE 291
QY 299 LRRTVQSLIEDLDSMRNLKASLENSLREVEARYALQMEQNGILHLHSESLAQTRAEGOR 358
DB 292 LRRTVQSLIEDLDSMRNLKASLENSLREVEARYALQMEQNGILHLHSESLAQTRAEGOR 351
QY 359 QAQYEALNKKVLEAEIATYRRLLEDGEDFNLGDALDSNSMOTIOKTTTRRIVDGKV 418
DB 352 QAQYEALNKKVLEAEIATYRRLLEDGEDFNLGDALDSNSMOTIOKTTTRRIVDGKV 411
QY 419 VSETNDTKVLRH 430
DB 412 VSETNDTKVLRH 423

RESULT 3

A28825

keratin, type I nonepidermal - African clawed frog

C/Species: Xenopus laevis (African clawed frog)

C/Date: 30-Jun-1989 #sequence revision 30-Jun-1989 #text_change 09-Jul-2004

C/Accession: A28825

R/Lafamme, S.E.; Jamrich, M.; Richter, K.; Sargent, T.D.; Dawid, I.B.

Genes Dev. 2, 853-862, 1988

A/Title: Xenopus endo B is a keratin preferentially expressed in the embryonic notochor

A/Reference number: A28825; MUID:89092007; PMID:2463213

A/Accession: A28825

A/Molecule type: mRNA

A/Residues: 1-368 <LAF>

A/Cross-references: UNIPROT:P08802; GB:Y00230; NID:g64863; PIDN:CAA68372.1; PID:g64864

C/Genetics:

A/Start codon: GGT

C/Superfamily: cytoskeletal keratin

C/Keywords: coiled coil

Query Match 53.7%; Score 1137.5; DB 2; Length 368;
Best Local Similarity 61.2%; Pred. No. 1e-48;
Matches 226; Conservative 74; Mismatches 58; Indels 11; Gaps 5;

QY 69 GGLAG-----MGIONKXETWQSLNDRLASVLDVRVSLTEENRRLSKIREHLEKKGQ 122
DB 2 GGFSGASNVNLFQGVQNEKETMQLNDRLASVLDVRVSLTESANKLEVQIRQTEKKGP- 60
QY 123 VRDMSHYFKIIEEDLRAQIFANTVDNARIVLQIDNARLAADDFRVKYTELAMROSVEN 182
DB 61 AKDMSPIYMTIEDLKQVNSIVENSQVLQIDNARLAADDFRVKYTESEVAIRMSVETI 120
QY 183 HGLRKVIDDNTNITRLQLETEIEALKEELLFMKKNHEEVEVKGLQAOIASGGLTVEVDAPK 242
DB 121 GGLRKVIDDNTNITRLQLETEIEALKEELLFMKKNHEEVEVKGLQAOIASVAVTEVDAPK 180
QY 243 QDLAKIMADIRAOYDELAARKNREELDKYWSQOIEESTVVTQSAAVGAETTLTELRT 302
DB 181 QDLGKIMADIRAOYDELAARKNREELDKYWSQOIEESTVVTQVNLDBALHTAKSSVTELRRT 240